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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/423,554 11/10/99 ARISTIDOU

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EXAMINER

WALICKA, M

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

07/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/423,554

Applicant(s).

ARISTIDOU ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 13-16, 24, 27, 31, 32 and 34-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 7-23, 25-26, 28-30, 33 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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The examiner acknowledges the election of claims. Applicants elected, with traverse, invention of Group I claims 1-10, 17-22, 25, 26, 28-30, 33 and 38 drawn and organism and method of production of ethanol. The traverse is on the ground that "the groups in which examiner placed the respective 'inventions' all have a common single special technical feature that makes a contribution over the prior art" and that "there is one unified idea that can be solved by different processes."

The examiner has not questioned the existence of the special technical feature shared by the claims, but indicated that the claims are drawn to four methods of production of four chemicals, whereas 37 CFR 1.475 does not provide for multiple products/methods within a single application. Therefore, restriction is proper and MADE FINAL.

Claims 1-38 are pending in the application. Claims 13-16, 24, 27, 31, 32, and 34-37 are withdrawn from consideration as directed to the nonelected inventions. Claims 1-10, 17-22, 25, 26, 28-30, 33 and 38 are the subject of this Office action.

Detailed Office Action

1. Objections

1.1. Specification

The specification is objected to for usage of the phrase: "recombinant molecule encoding or otherwise causing the expression of"; for example page 9, line 32. Encoding does not mean expressing. An enzyme may be encoded but never expressed.

In the title of Table 3 the control strain of *S. cerevisiae* is mentioned as H2189, whereas in the Table as H2186. Correction is necessary.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

1.2. Drawings

This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

2. Rejections

2.1. 35 USC 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-10, 17- 22, 28-30, 33 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 17 and 21 recite the following phrases that render the claim indefinite or confusing:

(a) "at least one recombinant DNA molecule encoding or otherwise causing the expression of at least one enzyme." This phrase renders the claim indefinite. Encoding does not mean expressing; an enzyme may be encoded but never expressed in cell or *in vitro*.

(b) " two pyrimidine nucleotide-linked dehydrogenase reactions with **different** specificities for the NAD/NADH and NADP/NADPH coenzyme couples". This phrase changes the inventors' idea. The idea is to exploit one or a pair of "dehydrogenases with **opposite [not different]** coenzyme specificities for NAD/NADH and NADP/NADPH" (page 10 line 1) so as to equilibrate the ratios of NAD/NADH and NADP/NADPH that are maintained different in living cells. On page 11 line 28 Applicants explain how this equilibration is achieved: "enzyme that catalyses at least one step of a cyclic series of reactions in which NADP is **reduced** to NADPH and NADH is **oxidized** to NAD, or *vice versa*."

(c) "so facilitates the transfer of electrons." This phrase is confusing. The examiner assumes that it is used to mean to equilibrate the transfer of electrons.

(d) the term "useful product" is indefinite. Therefore as long as Applicants do not provide their meaning of the term it renders the claim indefinite.

Dependent claims 2-10, 18-20, 22, 28-30, 33 and 38 are including into rejection because they do not correct deficiency of the claim from which they depend.

Claim 2, 6 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite, respectively:

"raw material",

"biotechnological process", and

"raw materials",

without defining them, therefore the claims are rendered indefinite.

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The term "required metabolic capacity" in claim 7 is a relative term which renders the claim indefinite. The term "required metabolic capacity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

2.2. 35 USC 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for glutamate dehydrogenase and malic enzyme from *S. cerevisiae*, does not reasonably provide enablement for any enzyme which is a pyridine nucleotide-linked dehydrogenase or any malate dehydrogenase or aldehyde dehydrogenase. Claims are so broad as to encompass any NAD/NADH and NADP/NADPH dependent dehydrogenase, or any malate dehydrogenase or aldehyde dehydrogenase from any organism and man-made. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims. The disclosure is limited to glutamate dehydrogenase and malic enzyme from *S. cerevisiae*.

While recombinant techniques are known, it is not routine in the art to screen for large numbers of dehydrogenases as encompassed by the instant claim when the results of obtaining transformants with claimed characteristics is unpredictable. The specification does not support the broad scope of the claim which encompass all possible NAD/NADH and NADP/NADPH dependent dehydrogenase, or any malate dehydrogenase or aldehyde dehydrogenase, from any organism and man-made because the specification provides insufficient guidance as to which of the essentially infinite choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including any of NAD/NADH and NADP/NADPH dependent dehydrogenase, or any malate dehydrogenase or aldehyde dehydrogenase, from any organism and man-made. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination which of extremely large number of transformants have the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

2.3. 35 USC, section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Boles et al (The role of the NAD-dependent glutamate dehydrogenase in restoring growth on glucose of a *Saccharomyces cerevisiae* phosphoglucose isomerase mutant, Eur. J. Biochem. 1993; 217:469-477).

Boles et al teach a transformed microorganism with one recombinant DNA molecule, that is with the DNA encoding NAD linked glutamate dehydrogenase, said microorganism is able to convert NAD plus NADPH into NADH plus NADP.

Claim 1 is directed to a microorganism transformed with at least one recombinant DNA molecule encoding at least one enzyme that causes the functional coupling of the oxidation and reduction of substrates by dehydrogenases with opposite specificities for NAD/NADH and NAD/NADPH. The broad scope of claim 1 includes the transformant taught by Boles and co-workers.

3. Allowable subject matter

Claims 25 and 26 would be allowable if the certification were provided that the biologic deposit meets the criteria set forth in 37 CFR 1.801-1.809. Applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposit will be maintained in public repository for a period of 30 years or five years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

Claims 2-10, 17-22, 25, 26, 29-30, 33 and 38 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is the examiner's statement of the reason for allowable subject matter. The Applicants disclose transformants of *S. cerevisiae* and *S. pombe* transformed by xylose reductase and xylitol dehydrogenase from *Pichia stipitis* and/or multiple copies of *S. cerevisiae* glutamate dehydrogenase or malic enzyme. They also

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disclose *S. cerevisie* transformants that contain in addition to xylose reductase and xylitol dehydrogenase from *Pichia stipitis* and/or multiple copies of *S. cerevisiae* glutamate dehydrogenase or malic enzyme genes, genes encoding xylulokinase. The transformants of both yeast species are engineered to metabolize efficiently xylose and other pentoses to produce efficiently ethanol with simultaneous reduction in production of CO₂. The transformants are not taught or obvious over the prior art.

The prior art made of record and not relied upon is considered pertinent to applicants' disclosure:


Jeffries et al, Strain selection, taxonomy, and genetics of xylose fermenting yeasts, in "*Enzyme Microb. Technol.*", **1994**, vol. 16, pages 922-932.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent Examiner



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